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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/713,017	11/16/2000	Andre Choulika	02356.0077-01	6042

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EXAMINER

EPPS, JANET L

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 02/22/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/713,017

Applicant(s)

CHOULIKA ET AL.

Examiner

Janet Epps

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 25-40 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1 and 25-40 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Claim Objections

1. Claim 26 is objected to because of the following informalities: Claim 26 recites the phrase "wherein said retroelements comprise cis-acting region," this phrase lacks the indefinite article "a" before the term "cis-acting." Appropriate correction is required.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 32-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 32-36 recite the limitation "said recognition site" in referring back to claim 25. There is insufficient antecedent basis for this limitation in the claim. Claim 25 recites a "recognition sequence."

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 39 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Biological material need not be deposited unless access to such material is necessary for the satisfaction of the statutory requirements for patentability under 35 USC

112. If a deposit is necessary, it shall be acceptable if made in accordance with these regulations. Biological material need not be deposited, *inter alia*, if it is known and readily available to the public or can be isolated without undue experimentation. In the present case applicants claim the deposited biological material by its accession number. In order for the skilled artisan to practice the claimed invention therefore, said skilled artisan would need to have unrestricted access to the deposited material. However, the specification as filed does not state that all restrictions on the deposits will be irrevocably removed on issuance of a patent and that the deposit will be replaced if the depository cannot dispense viable samples.

In the absence of evidence showing that the plasmid having the accession no. I-1599 as recited in claim 39 is publicly available (i.e., deposited in compliance with 37 CFR 1.801-1.809), or can be isolated without undue experimentation, claim 39 is not supported by an enabling disclosure.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 25-26, 29-32, 37 and 40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,200,800. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the issued patent and the claims 25-26, 29-32, 37 and 40 of the instant application are drawn to a nucleic acid molecule and a retroviral vector comprising retroelements that comprise a recombinant provirus, a nucleotide sequence of interest, and a recognition sequence for the elimination of proviral sequences in the recombinant provirus. However, although the claims of the issued patent and those of the instant application read on overlapping subject matter, the claims of the instant application are broader in scope than those recited in the issued patent. The claims of the issued patent represent a distinct species of the broader genus of nucleic acid molecules and retroviral vectors encompassed by the instant claims. The claims of the issued patent are further limited to a defined class of retroviral vector, namely wherein the vector is a defective Moloney murine leukemia virus, and wherein the recognition sequence in said virus is in a U3 region of its 3' LTR, or in a U5 region of its 5' LTR.

According to MPEP § 2131.02, "A generic claim cannot be allowed to an applicant if the prior art discloses a species falling within the claimed genus." The species in that case will anticipate or render obvious the claimed genus. Therefore, the distinct species of retroviral vector and nucleic acid molecules recited in the issued patent render

obvious the claims drawn to a broad genus of retroviral vector and nucleic acid molecules as recited in the instant application.

See also MPEP § 804, which states, "[I]f the application at issue is the later filed application or both are filed on the same day, only a one-way determination of obviousness is needed in resolving the issue of double patenting, i.e., whether the invention defined in a claim in the application is an obvious variation of the invention defined in a claim in the patent. See, e.g., *In re Berg*, 46 USPQ2d 1226 (Fed. Cir. 1998) (the court applied a one-way test where both applications were filed the same day). If a claimed invention in the application is obvious over a claimed invention in the patent, there would be an unjustified timewise extension of the patent and an obvious-type double patenting rejection is proper." In the present case, the instant application represents the later filed application, therefore only a one-way determination of obviousness is required.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 25-38 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guild et al. (WO92/07943), in view of Enquist et al. (EP-A-0300422), and Anderson et al. (US Patent 5,629,159).

Applicants claim a nucleic acid molecule comprising retroelements comprising recombinant retrovirus, wherein the nucleic acid molecule contains a nucleotide sequence

of interest that can be integrated with the retrovirus, and further contains a recognition sequence for a recombinase. The sequence of interest is integrated into the cis acting region of the retroviral element (the long terminal repeat or LTR), where it is integrated into either the 5' or 3' LTR, the vector may further encode the recombinase, which is the CRE protein of bacteriophage P1 and the recognition sequence encodes a loxP element, the sequence required for recombination events directed by the Cre recombinase. The sequence of interest may encode a polypeptide, an antisense RNA or a ribozyme.

Guild discloses a replication defective retroviral vector (possessing 5' and 3' LTR sequences), which has a sequence of interest inserted into the cis acting region of the virus (LTR; page 16, lines 20-24). Guild teaches each and every aspect of the instant vectors except the inclusion of loxP elements and the Cre recombinase.

Enquist discloses the desirability of using recombination as a means of modifying retroviral vectors (page 5, lines 43-57; and page 7, lines 26-39). A viral vector is modified by the insertion of loxP elements (page 5, lines 1-26) and the loxP element so included is a recognition sequence for the bacteriophage P1 Cre recombinase, which is disclosed as either inserting sequences into the viral vector, and/or removing sequences from the vector (page 9, lines 1-5). The sequence of interest may encode a polypeptide. However, Enquist does not disclose such a vector wherein the CRE enzyme is encoded within the vector itself.

Anderson discloses retroviral vector constructions (see figures 1a-1d and 2a-b) which contain LTR elements, which express sequences of interest that are integrated into a cis acting region of the virus, which encodes selectable markers, and which has promoters and other control elements. Such vectors were modified to contain loxP

elements (fig. 2a-b) for the removal of an intervening nucleotide sequence. The use of the Cre/loxP and FLP/FRT recombinase systems is disclosed (col. 7, lines 20-28) and the gene encoding the recombinase (either Cre or FLP) is part of the retroviral construct *col. 8, lines 38-56). The desirability of removing or eliminating the recombinase by the recombination event, along with a sequence of interest, is further disclosed (col. 8, lines 47-52). Furthermore, Anderson also describes the use of replication defective retroviral vectors (col. 11, lines 41-67).

In seeking to express a protein using retroviral vectors, one of ordinary skill in the art at the time of filing of the instant application would have been motivated to combine the teachings of Guild with regards to replication deficient retroviral vectors with the teachings of Enquist with regard to the utility of recombination as a means for preparing and modifying vectors of all types, including retroviral vectors, for the known and expected property of effective insertion or removal of a sequence of interest into or from the vector. One would have been motivated to further combine the teachings of Anderson with regard to encoding the recombinase directly into the retroviral vector, for the known and expected property disclosed by Anderson, namely simultaneous removal of the recombinase enzyme along with the sequence of interest. In so doing, one of skill in the art would have prepared a recombinant vector that would integrate into the genome, wherein one could then inducibly (Anderson; col. 8, lines 38-55) remove sequences integrated into the genome by the retroviral vector, along with the recombinase. Given the teachings of the prior art and the knowledge of one of ordinary skill in the art, it must be considered that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Therefore, the invention as a whole was prima face obvious at the time of filing over Guild in view of Enquist et al. and Anderson et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L Epps whose telephone number is 703-308-8883. The examiner can normally be reached on M-T, Thurs-Friday 8:30AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703)-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-746-5143 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L Epps
Examiner
Art Unit 1635

JLE
February 19, 2002


SEAN MCGARRY
PRIMARY EXAMINER